REMARKS

Amendments to the Claims

Claims 6 and 26 have been canceled. Claims 1, 3, 4, 5, 7, 8, 21, 23, 24, 25, 27, 28, 60, 70 and 89 have been amended.

Claims 1, 70 and 89 have been amended to recite "wherein the anti-resorptive agent is a highly specific cytokine antagonist that inhibits TNF-α." Claim 21 has been amended to recite "wherein the highly specific cytokine antagonist inhibits TNF-α". Support for these amendments is found in the specification, for example, at page 29, lines 8-9.

Claims 3, 4, 5, 7, 8, 23, 24, 25, 27 and 28 have been amended to alter their dependency.

Claim 60 has been amended to recite "A method of treating an osteoporotic patient having a spinal unit comprising an upper vertebral body, a lower vertebral body, and an intervertebral disc therebetween, comprising the steps of: a) inserting a device into at least one vertebral body adjacent to the intervertebral disc, wherein the device is adapted to deliver an effective amount of a bone forming agent into the vertebral body, b) removing at least a portion of the intervertebral disc to create a disc space, and c) inserting a spinal implant into the disc space." Support for this amendment is found in the specification, for example, at page 7, lines 1-22, at page 13, lines 14-17, and at page 53, line 21-page 54, line 19.

No new matter has been added. Therefore, entry of these amendments into the application is respectfully requested.

Amendments to the Specification

As requested by the Examiner, Applicants have reviewed the use of trademarks within the specification. Applicants' review of the specification indicates that all trademarks listed within the specification do comply with the requirements.

Rejection of Claim 60 under 35 U.S.C. § 102(b)

The Examiner has rejected Claim 60 under 35 U.S.C. § 102(b) as being unpatentable over Trieu *et al.* (US 2002/0026244). The Examiner states that Trieu *et al.* teaches methods of

implanting nucleus pulposus implants which may contain growth factors and steroids for treating osteoporosis.

Applicants respectfully disagree. Generally, all of the elements of the claimed invention must be found within a single reference in order to anticipate, either expressly or inherently, under 35 U.S.C. §102(b). As stated in *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986), for example, "[i]t is axiomatic that for prior art to anticipate under §102 it has to meet every element of the claimed invention, and that such a determination is one of fact."

Applicants' claimed invention, as amended, is directed to a method of treating an osteoporotic patient, comprising inserting a device into at least one vertebral body adjacent to the problematic intervertebral disc. As taught in Applicants' specification, such a device would prevent natural endplates adjacent to the disc from subsiding into a replacement intervertebral implant, thereby decreasing the height of the disc space (See Specification, page 53, line 21-page 54, line 13). A benefit of preventing such subsidence is largely due to the fact that the function of the implant is to restore the natural spacing between the vertebrae, thereby restoring the natural geometric relationships of the different parts of the spine. Subsidence around the implant acts to decrease the spacing between the vertebrae and so represents a deviation from the natural geometric relationships of the different parts of the spine. The method of Claim 60 would help prevent such subsidence.

Trieu *et al.* discloses a method to replace a natural nucleus pulposus with a nucleus pulposus implant [0007] and [0109]. Trieu *et al.* discloses a method to implant a nucleus pulposus implant [0109] that may contain a growth factor [0101]. Trieu *et al.* does not disclose a device, adapted to deliver a bone forming agent, that is inserted into a vertebral body adjacent to the intervertebral disc. Therefore, Trieu *et al.* does not teach all elements of Claim 60.

Thus, Trieu *et al.* does not anticipate the claimed invention. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-10, 21-30, 70 and 89 under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 1-10, 21-30, 70 and 89 under 35 U.S.C. § 103(a) as being unpatentable over Radomsky (US 5,942,499) in view of Boyle *et al.* (US 2003/0207827).

The Examiner states that Radomsky teaches a bone growth-promoting composition comprising growth factors. In addition, the Examiner states that Boyle *et al.* teaches methods to treat osteoporosis comprising osteoprotegrin.

Applicants respectfully disagree. As amended, Applicants' invention is directed to a method of therapeutically treating a patient, comprising locally administering a bone forming agent into the bone, and administering an anti-resorptive agent into the bone, wherein the anti-resorptive agent is a highly specific cytokine antagonist, such as an antagonist that inhibits TNF-α.

Amended Claim 1 of Applicants' invention is directed to a method of therapeutically treating an uncoupled resorbing bone in a patient, comprising locally administering a first formulation comprising a bone forming agent into the bone, and locally administering a second formulation comprising an anti-resorptive agent into the bone, wherein the anti-resorptive agent is a highly specific cytokine antagonist, such as an antagonist that inhibits TNF-α.

Amended Claims 21 and 70 are directed to treating osteoporosis in a patient, comprising locally administering an effective amount of a formulation comprising a highly specific cytokine antagonist into bone, wherein the highly specific cytokine antagonist inhibits TNF-α. Claim 89 is directed to a method of therapeutically treating a patient, comprising locally administering a first formulation comprising a bone forming agent into the bone, and systemically administering an effective amount of a second formulation comprising an anti-resorptive agent into the bone, wherein the anti-resorptive agent is a highly specific cytokine antagonist that inhibits TNF-α.

As discussed in Applicants' specification, the prior art does not disclose the intraosseous injection of a highly specific cytokine antagonist to increase the bone mineral density of the uncoupled resorbing bone. See, for example, at page 4, lines 11-13.

Applicants recognized benefits of such local administration. For example, since a high specificity cytokine antagonist (HSCA) inhibits only the specific cytokine(s) of interest, the HSCA may be combined with other therapeutic agents that can also be injected into the bone without reducing the effectiveness of those other agents.

Radomsky discloses a composition comprising hyaluronic acid and a growth factor to promote bone growth. In addition, Radomsky discloses that the composition can be applied to the desired site of bone growth. Radomsky does not teach or suggest administration of an anti-

resorptive agent or a highly specific cytokine antagonist, such as an antagonist that inhibits TNF-α.

Boyle discloses that osteoprotegerin can be used to treat bone disease. Osteoprotegerin is a member of the tumor necrosis factor receptor (TNFR) superfamily and it binds a receptor activator of NF-kB ligand (RANK-ligand). According to Boyle, it is closely related to TNFR-2 and, thus, may negatively regulate its ligand. Boyle tested administration of osteoprotegerin to inhibit the effects of IL-1 alpha and beta. Boyle does not teach or suggest local administration of a highly specific cytokine antagonist, such as a highly specific cytokine antagonist that inhibits TNF-α.

The references in combination do not teach or suggest Applicant's invention comprising local administration of a bone forming agent and administration, including local administration, of a highly specific cytokine antagonist that inhibits TNF-α, in order to treat an uncoupled resorbing bone. Therefore, Applicants' claimed invention is more than a predictable variation of what was known in the art and the invention is not obvious.

Reconsideration and withdrawal of the rejection are respectfully requested.

Supplemental Information Disclosure Statement

Applicants respectfully request the Examiner to consider and acknowledge the references listed on page 3 of the Information Disclosure Statement filed on October 13, 2005. Applicants also respectfully request the Examiner to consider and acknowledge the references listed in the 1449-Form filed with the Information Disclosure Statement filed on May 16, 2007.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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